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<110> Matsumoto, Yoh-Ichi
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TEIJIN LIMITED

<120> HUMANIZED ANTIBODIES THAT RECOGNIZE VEROTOXIN II AND
CELL LINE PRODUCING SAME

<130> 019026-000110US

<140> 09700851
<141> 2003-11-03

<150> WO 99/59629
<151> 1999-05-19

<150> US 60/086,570
<151> 1998-05-20

<160> 10

<170> PatentIn Ver. 2.1

<210> 1
<211> 414
<212> DNA
<213> Mus musculus

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<221> CDS
<222> (1)..(414)

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<223> Figure 1(A): Heavy chain variable region of mouse
antibody VTm1.1 (MuVTm1.1).

<400> 1
atg aac ttt gtg ctc agc tcg att ttc ctt gcc ctc att tta aaa gga 48
Met Asn Phe Val Leu Ser Ser Ile Phe Leu Ala Leu Ile Leu Lys Gly
1 5 10 15

gtc cag tgt gaa gtg cag ctg gtg gag tcg ggg gga ggc tta gtg aag 96
Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
20 25 30

cct gga ggg ccc ctg aaa ctc tcc tgt gca gcc tct gga ttc act ttc 144
Pro Gly Pro Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

agt agt tat ggc atg tct tgg gtt cgc cag act ccg gag aag agg ctg 192
Ser Ser Tyr Gly Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu

50	55	60	
gag tgg gtc gca acc att agt act ggt ggt agt tac acc tac tac cca Glu Trp Val Ala Thr Ile Ser Thr Gly Gly Ser Tyr Thr Tyr Tyr Pro			240
65	70	75	80
gac agt gtg aag ggt cga ttc acc atc tcc aga gac aat gcc aag aac Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn			288
85	90	95	
gcc ctg tat ctg caa atg agc agt ctg agg tct gag gac acg gcc ata Ala Leu Tyr Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile			336
100	105	110	
tat tac tgt gca aga cgg ggg gac gca tgg ggt aac ttg gac tac tgg Tyr Tyr Cys Ala Arg Arg Gly Asp Ala Trp Gly Asn Leu Asp Tyr Trp			384
115	120	125	
ggt caa gga acc tct gtc acc gtc tcc tca Gly Gln Gly Thr Ser Val Thr Val Ser Ser			414
130	135		
<210> 2			
<211> 138			
<212> PRT			
<213> Mus musculus			
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<223> Figure 1(A): Heavy chain variable region of mouse antibody VTm1.1 (MuVTm1.1).			
<400> 2			
Met Asn Phe Val Leu Ser Ser Ile Phe Leu Ala Leu Ile Leu Lys Gly			
1	5	10	15
Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Lys			
20	25	30	
Pro Gly Gly Pro Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe			
35	40	45	
Ser Ser Tyr Gly Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu			
50	55	60	
Glu Trp Val Ala Thr Ile Ser Thr Gly Gly Ser Tyr Thr Tyr Tyr Pro			
65	70	75	80
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn			
85	90	95	
Ala Leu Tyr Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile			
100	105	110	
Tyr Tyr Cys Ala Arg Arg Gly Asp Ala Trp Gly Asn Leu Asp Tyr Trp			
115	120	125	

Gly Gln Gly Thr Ser Val Thr Val Ser Ser
130 135

<210> 3
<211> 381
<212> DNA
<213> Mus musculus

<220>
<221> CDS
<222> (1)..(381)

<220>
<223> Figure 1(B): Light chain variable region of mouse
VTm1.1 antibody (MuVTm1.1).

<400> 3
atg gtt ttc aca cct cag ata ctt gga ctt atg ctt ttt tgg att tca 48
Met Val Phe Thr Pro Gln Ile Leu Gly Leu Met Leu Phe Trp Ile Ser
1 5 10 15

gcc tcc aga ggt gat gtt gtg cta act cag tct cca gcc acc ctg tct 96
Ala Ser Arg Gly Asp Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
20 25 30

gtg act cca gga gat agc gtc agt ctt tcc tgc agg gcc agt caa act 144
Val Thr Pro Gly Asp Ser Val Ser Leu Ser Cys Arg Ala Ser Gln Thr
35 40 45

att agc aac aac cta cac tgg tat caa cac aaa tca cat gag tct cca 192
Ile Ser Asn Asn Leu His Trp Tyr Gln His Lys Ser His Glu Ser Pro
50 55 60

agg ctt ctc atc aag tct gct tcc cag tcc atc tct ggg atc ccc tcc 240
Arg Leu Leu Ile Lys Ser Ala Ser Gln Ser Ile Ser Gly Ile Pro Ser
65 70 75 80

agg ttc agt ggc agt gga tca ggg aca gat ttc act ctc agt atc aac 288
Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn
85 90 95

agt gtg gaa act gaa gat ttt gga atg tat ttc tgt caa cag agt tac 336
Ser Val Glu Thr Glu Asp Phe Gly Met Tyr Phe Cys Gln Gln Ser Tyr
100 105 110

agc tgg ccg ctc acg ttc ggt gct ggg acc aag ctg gag ctg aaa 381
Ser Trp Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
115 120 125

<210> 4
<211> 127
<212> PRT
<213> Mus musculus

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<223> Figure 1(B): Light chain variable region of mouse
VTm1.1 antibody (MuVTm1.1).

<400> 4

Met Val Phe Thr Pro Gln Ile Leu Gly Leu Met Leu Phe Trp Ile Ser
1 5 10 15

Ala Ser Arg Gly Asp Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
20 25 30

Val Thr Pro Gly Asp Ser Val Ser Leu Ser Cys Arg Ala Ser Gln Thr
35 40 45

Ile Ser Asn Asn Leu His Trp Tyr Gln His Lys Ser His Glu Ser Pro
50 55 60

Arg Leu Leu Ile Lys Ser Ala Ser Gln Ser Ile Ser Gly Ile Pro Ser
65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn
85 90 95

Ser Val Glu Thr Glu Asp Phe Gly Met Tyr Phe Cys Gln Gln Ser Tyr
100 105 110

Ser Trp Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
115 120 125

<210> 5

<211> 414

<212> DNA

<213> Mus musculus

<220>

<221> CDS

<222> (1)..(414)

<220>

<223> Figure 2(A): Heavy chain variable region of
humanized VTm1.1 antibody (HuVTm1.1).

<400> 5

atg aac ttt gtg ctc agc tcg att ttc ctt gcc ctc att tta aaa gga 48
Met Asn Phe Val Leu Ser Ser Ile Phe Leu Ala Leu Ile Leu Lys Gly
1 5 10 15

gtc cag tgt gaa gtg caa ctg gtg gag tcg ggg gga ggc tta gtg cag 96
Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln
20 25 30

cct gga ggg tcc ctg aga ctc tcc tgt gca gcc tct gga ttc act ttc 144
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

agt agt tat ggc atg tct tgg gtt cgc cag gct ccg ggt aag ggt ctg		192
Ser Ser Tyr Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu		
50	55	60
gag tgg gtc gca acc att agt act ggt ggt agt tac acc tac tac cca		240
Glu Trp Val Ala Thr Ile Ser Thr Gly Gly Ser Tyr Thr Tyr Tyr Pro		
65	70	75
		80
gac agt gtg aag ggt cga ttc acc atc tcc aga gac aat tcc aag aac		288
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn		
85	90	95
acc ctg tat ctg caa atg aac agt ctg agg gct gag gac acg gcc gta		336
Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val		
100	105	110
tat tac tgt gca aga cgg ggg gac gca tgg ggt aac ttg gac tac tgg		384
Tyr Tyr Cys Ala Arg Arg Gly Asp Ala Trp Gly Asn Leu Asp Tyr Trp		
115	120	125
ggt caa gga acc tta gtc acc gtc tcc tca		414
Gly Gln Gly Thr Leu Val Thr Val Ser Ser		
130	135	

<210> 6
<211> 138
<212> PRT
<213> Mus musculus

<220>
<223> Figure 2(A): Heavy chain variable region of
humanized VTm1.1 antibody (HuVTm1.1).

Met Asn Phe Val Leu Ser Ser Ile Phe Leu Ala Leu Ile Leu Lys Gly		
1	5	10
		15
Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln		
20	25	30
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe		
35	40	45
Ser Ser Tyr Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu		
50	55	60
Glu Trp Val Ala Thr Ile Ser Thr Gly Gly Ser Tyr Thr Tyr Tyr Pro		
65	70	75
		80
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn		
85	90	95
Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val		
100	105	110
Tyr Tyr Cys Ala Arg Arg Gly Asp Ala Trp Gly Asn Leu Asp Tyr Trp		

115

120

125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
130 135

<210> 7
<211> 381
<212> DNA
<213> Mus musculus

<220>
<221> CDS
<222> (1)..(381)

<220>
<223> figure 2(B): Light chain variable region of
humanized VTm1.1 antibody (HuVTm1.1) .

<400> 7
atg gtt ttc aca cct cag ata ctt gga ctt atg ctt ttt tgg att tca 48
Met Val Phe Thr Pro Gln Ile Leu Gly Leu Met Leu Phe Trp Ile Ser
1 5 10 15
gcc tcc aga ggt gaa att gtg cta act cag tct cca gcc acc ctg tct 96
Ala Ser Arg Gly Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
20 25 30
gtg tct cca gga gaa aga gcc act ctt tcc tgc agg gcc agt caa act 144
Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr
35 40 45
att agc aac aac cta cac tgg tat caa caa aaa cca ggt cag gct cca 192
Ile Ser Asn Asn Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
50 55 60
agg ctt ctc atc aag tct gct tcc cag tcc atc tct ggg ata ccc gcc 240
Arg Leu Leu Ile Lys Ser Ala Ser Gln Ser Ile Ser Gly Ile Pro Ala
65 70 75 80
agg ttc agt ggc agt gga tca ggg aca gat ttc act ctc act atc agc 288
Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
85 90 95
agt ctg gaa tct gaa gat ttt gca gtg tat tac tgt caa cag agt tac 336
Ser Leu Glu Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Tyr
100 105 110
agt tgg ccg ctc acg ttc ggt caa ggg acc aag gtg gag atc aaa 381
Ser Trp Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
115 120 125

<210> 8
<211> 127
<212> PRT

<213> Mus musculus

<220>

<223> Figure 2(B): Light chain variable region of
humanized VTm1.1 antibody (HuVTm1.1) .

<400> 8

Met Val Phe Thr Pro Gln Ile Leu Gly Leu Met Leu Phe Trp Ile Ser
1 5 10 15

Ala Ser Arg Gly Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
20 25 30

Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr
35 40 45

Ile Ser Asn Asn Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
50 55 60

Arg Leu Leu Ile Lys Ser Ala Ser Gln Ser Ile Ser Gly Ile Pro Ala
65 70 75 80

Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
85 90 95

Ser Leu Glu Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Tyr
100 105 110

Ser Trp Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
115 120 125

<210> 9

<211> 123

<212> PRT

<213> Homo sapiens

<220>

<223> heavy chain variable region of the GF4/1.1 antibody

<400> 9

Glu Val Gln Val Leu Glu Ser Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Ala Ser Gly Glu Asn Thr Tyr Tyr Ala Asp Pro Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Val Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Lys Gly Gly Arg Gln Trp Val Val Leu Gly Tyr Phe Phe Asp Ser
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 10
<211> 110
<212> PRT
<213> Homo sapiens

<220>
<223> light chain variable region of the GF4/1.1 antibody

<400> 10
Glu Ile Leu Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15
Glu Arg Val Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Ser
65 70 75 80
Glu Asp Phe Ala Leu Tyr Tyr Cys His Glu Tyr Asn Gly Trp Pro Pro
85 90 95
Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr
100 105 110